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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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JOHN S. PRATT, ESQ
KILPATRICK STOCKTON, LLP
1100 PEACHTREE STREET
SUITE 2800
ATLANTA, GA 30309

EXAMINER
ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,333	PHILLIPS ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,11-14 and 16-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,11-14 and 16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed May 31, 2002 (Paper No. 9) has been entered. Claims 3-10 and 15 have been canceled. New claims 17-21 have been added.

Claims 1, 2, 11-14 and 16-21 are pending in the application and are examined herein.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 2, 11-14 and 16-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4, 9, 10 and 11 of U.S. Patent No. 6,326,357 (here after referred to as '357). Although the conflicting claims are not identical, they are not patentably distinct from each other because both are drawn to methods of treatment comprising administration of a composition comprising Mycobacterium cell wall complex (MCC) (e.g. M. phlei cell wall complex) wherein the Mycobaterium DNA (M-DNA) is preserved and complexed on the MCC. Claims 3, 4, 9, 10 and 11 of '357 are drawn to a method of treating cancer, while the claims of the instant application are drawn to methods of treating and preventing inflammation, therefore an obvious–type double patenting rejection is

appropriate. Although the claims of '357 are drawn to methods of treating a different disorder (cancer), the method steps are identical to those of the instant application. Specifically, both methods encompass administration of a composition comprising MCC wherein M-DNA is preserved and complexed on the MCC and a pharmaceutically acceptable carrier. Furthermore, the concentration of the MCC composition that is administered is the same (see the instant application p. 7, line 2, which teaches that the most preferred concentration of the therapeutic composition is in a range from about 0.001-10mg/kg per dose, and Example 3 which teaches administration of 6.7 mg/kg MCC). Also, '357 defines the preferred range of MCC administration as from about 0.001mg/kg to about 10mg/kg per dose (column 9, lines 50-55), and specifically defines a treatment of MCC at 6.6mg/kg (see column 19, lines 10-14). Additionally, '357 claim 11 indicates that the treatment stimulates the production of IL-10. It was known in the art that IL-10 is an anti-inflammatory cytokine that has the ability to inhibit macrophage and Type-1 helper T-cell functions, as evidenced by Bermudez et al. (Infect. Immun. July 1993; see p. 3093, paragraph traversing col. 1-2; and p. 3096, left col.). Therefore, it would have been obvious that treatment with MCC would be effective for treating and preventing inflammation.

Response to Arguments

3. Applicant's arguments filed May 31, 2002 have been fully considered but they are not persuasive.

Applicants argue that claim 1 of '357 is drawn to a composition, not a method of treatment. It is acknowledged that claim 1 of '357 is drawn to a composition. However, claims 3, 4, 9, 10 and 11 of '357 are drawn to methods of treatment using MCC, as mentioned above,

and, therefore, the instant claims are obvious over the claims 3, 4, 9, 10 and 11 of '357 as set forth above.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bermudez & Champsi (Infect. Immun. July 1993; Vol. 61, No. 7; p. 3093-3097).

Bermudez & Champsi teaches Mycobacterium avium induces production of IL-10 in mice (see abstract, p. 3093; Table 1, p. 3095). IL-10 is an anti-inflammatory cytokine that has the ability to inhibit macrophage and Type-1 helper T-cell functions (see p. 3093, paragraph traversing col. 1-2; and p. 3096, left col.). Of particular interest, Bermudez & Champsi state, " [T]he antagonistic effect of IL-10 can play an important role in the kinetics of cytokine response following infection with M. avium" and "suppressive cytokines can be advantageous to the bacterium" (see p. 3096, left col.). Therefore, Bermudez & Champsi teach a method of administering to an animal an effective amount of a composition comprising a mycobacterial DNA preserved and complexed on a mycobacterial cell wall and a liquid pharmaceutically acceptable carrier wherein the effective amount is effective to induce the synthesis of cytokine IL-10. This method would effectively treat or prevent inflammation in an animal because the mycobacterium administered is effective to induce the synthesis of anti-inflammatory cytokine IL-10.

Response to Arguments

6. Applicant's arguments filed May 31, 2002 have been fully considered but they are not persuasive.

Applicants argue that the cited reference teaches the administration of live mycobacterium, while the instant claims are drawn to administration of BCC which is made from disrupted mycobacterium and does not contain any live mycobacterium. Applicants indicate that Examples 1 and 2 of the specification supports this notion.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that BCC does not comprise living mycobacteria) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The cited reference meets each limitation of the claims. It is also respectfully pointed out that Example 1 of the specification teaches the method for producing MCC, which is a species of the genus BCC. Neither Examples 1 or 2 indicate that BCC is produced by disruption of mycobacterium, nor is there any indication that BCC does not comprise living mycobacteria.

7. The rejection of the claims under 35 U.S.C. 102(b) as being anticipated by Moura & Moriano has been withdrawn in view of applicants argument.

8. Claim 15 has been cancelled. Therefore the rejections of claim 15 are moot.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 2 and 11-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating inflammation comprising administration of a mycobacterial cell wall complex derived from M. phlei and M. avium, does not reasonably provide enablement for method for treating inflammation comprising administration of a mycobacterial cell wall complex derived from any other mycobacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404:
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn methods for treating and preventing inflammation comprising administration of a mycobacterial cell wall extract (i.e. BCC) to a subject in an

amount effective for the treatment or prevention of inflammation. Therefore, the nature of the invention is therapeutic treatment of disease.

The breadth of the claims

The breadth of the claims is very broad. For instance, the claims encompass the administration of a mycobacterial cell wall complex wherein the complex can be a cell wall complex from any species of mycobacterium. Furthermore, the claims encompass treating any type of inflammatory disorder in any species of animal, including humans.

The unpredictability of the art and the state of the prior art

The therapeutic treatment of disease is recognized as an unpredictable art. For instance, the court has recognized that physiological activity, which encompasses the therapeutic treatment of disease, is unpredictable. (See *In re Fisher*, 166 USPQ 18 (CCPA 1970)). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. (see *In re Fisher*, 166 USPQ 18 (CCPA 1970)). Here, it is unpredictable that a cell wall complex of any mycobacterium other than M. phlei and M. avium would function as an effective treatment for inflammation. This is because the art recognizes that there are substantial differences between the different species of mycobacteria, especially with regards to their effect on the immune system. For instance, Beltan et al. (Microbial Pathogenesis Vol. 28:313-318; 2000) teaches that infecting human macrophages with different species of live and heat-killed mycobacteria (including M. phlei, M. kansaii, M. smegmatis, M. avium, M. xenopi, and M. tuberculosis)

results in differential secretion of cytokines from the macrophages (see abstract and p.315, Figures 1 and 2). Therefore, the effect of cell wall complexes of different mycobacterial species cannot be accurately predicted.

To overcome the teachings in the art, the specification would need to supply direct evidence that administration of BCC from a representative number of species of mycobacteria would result in the prevention and treatment of inflammation; a disclosure that is not present in the specification.

Working Examples and Guidance in the Specification

The specification only discloses the treatment and prevention of inflammation in mice (see Examples 3-5, p. 8-10) and the treatment of osteoarthritis and colitis in humans (see Examples 6 and 7, p. 10) using only MCC (a mycobacterial cell wall complex of M. phlei). The specification does not teach the treatment or prevention of inflammation using a BCC of any mycobacterium other than MCC (M. phlei cell wall complex). Furthermore, there is no guidance regarding the appropriate dosage of any BCC other than MCC.

Quantity of Experimentation

The quantity of experimentation in this area is large since determination of the efficacy of every possible BCC (i.e. BCC of every species of mycobacteria) would require trial and error testing of every possible BCC in animal models, an unpredictable undertaking in itself. After successful experimentation in the animal models, the efficacy of the treatment would have to be tested in human subjects.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the high degree of unpredictability recognized in the art, the breadth of the claims, the limited number of working examples and guidance in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed method is undue.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne-Marie Baker
ANNE-MARIE BAKER
PATENT EXAMINER

J. Eric Angell
August 23, 2002